REMARKS

Claims 1-7, and 12 are rejected. Claims 1 and 12 are amended. Claims 8-11, and 13 are withdrawn. Claims 1-13 are pending. Reconsideration is respectfully requested in light of the amended claims and the following remarks.

I. Claim Rejections – 35 USC § 112, first paragraph, written description

Claims 1-7, 12, are rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants traverse the rejection.

In the interest of expediting prosecution, Applicants deleted reference to the phrase "or mutants or fragments thereof" in claim 1. Applicants, none the less, are of the view that the claims are not limited to the specific sequences recited in the instant application. The rejection is now moot and Applicants respectfully request the withdrawal of the rejection.

II. Claim Rejections – 35 USC § 112, first paragraph, scope of enablement

Claims 1-7, 12, are rejected under 35 U.S.C. § 112, first paragraph, for allegedly "not reasonably provide enablement for a polypeptide-dimer as recited in claim 1 comprising two soluble gp130 molecules, and wherein at least one of said soluble gp130 molecules is covalently linked to polyethylene glycol and wherein each of said soluble gp 130 molecules consists of the extracellular domains D 1-D3 of gp 130 or mutants or fragments thereof that maintain the ability to inhibit the activity of the agonistic complex IL-6-sIL-6R." Applicants traverse the rejection.

In the interest of expediting prosecution, Applicants deleted reference to the phrase "or mutants or fragments thereof" in claim 1. Applicants, none the less, are of the view that the claims are not limited to the specific sequences recited in the instant application. The rejection is now moot and Applicants respectfully request the withdrawal of the rejection.

Furthermore, Applicants note that the Examiner has acknowledged the enablement of a polypeptide-dimer comprising two soluble gp130 molecules comprising the amino acid sequence SEQ ID NO:2, wherein at least one of the soluble gp130 molecules is covalently linked to PEG.

Applicants respectfully assert that the enabled molecule is but one species in the genus of IL-6/sIL-6R inhibitors all of which contain as a core feature the extracellular domains D1-D3 of gp130. Therefore, Applicants contend that claim 1 is enabled as presently amended.

III. Claim Rejections – 35 U.S.C. § 112, second paragraph

Claims 1-7, and 12, are rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants traverse the rejection.

Claim 1

"fragments"

The rejection is now moot as the term "fragments" was deleted.

"Il-6/sIL-6R"

The rejection is now moot as the term "Il-6/sIL-6R" was amended to read "IL-6/sIL-6R."

Since the above terms were deleted or amended, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. § 112, second paragraph, be withdrawn.

Claim 12: "polypeptide-dimer"

Claim 12 is amended to include a hyphen inserted between the words "polypeptide" and "dimer." Additionally, the phrase "in a pharmaceutically acceptable carrier" was added. Subsequently, Applicants respectfully request that the rejection of claim 12 under 35 U.S.C. § 112, second paragraph, be withdrawn.

Claims 6 and 7

Claim 1 is amended as requested, consequently, claims 6 and 7 are not vague and indefinite. Therefore, Applicants respectfully request that the rejection of claims 6 and 7 under 35 U.S.C. § 112, second paragraph, be withdrawn.

IV. Claim Rejections – 35 U.S.C. § 102

Claims 1-5, 12 are rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by EP 1148065 A1 (2001). More specifically, the reference is alleged to teach "a polypeptide-dimer and a pharmaceutical composition thereof comprising two soluble gp130 molecules, wherein at least

one of said soluble gp130 molecules is covalently linked to polyethylene glycol and wherein each of said soluble gp130 molecules consists of the extracellular domains of D1-D3 of gp130." Applicants traverse the rejection.

Applicants respectfully assert that EP 1148065 A1 discloses the use of two soluble gp130 molecules. (Abstract; paragraphs 0001 and 0014; and Figure 1) The extracellular domain of gp130 consists of **6** domains (Figure 1 and Exhibit 1). In contrast, the claims of the instant invention recite a polypeptide-dimer wherein each soluble gp130 molecule consists of **3** extracellular domains, the D1-D3 domains.

Therefore, the chemical structures of the fusion proteins disclosed in EP 1148065 A1 and the soluble gp130 molecules of the instant application are not identical. The IL-6/sIL-6R complex inhibitory molecules recited in the claims of the instant invention comprise of two soluble gp130 molecules that contain only half of the gp130 extracellular domains. The use of inhibitory molecules that comprise of only half of the gp130 extracellular domains is not disclosed or even suggested by EP 1148065 A1.

Furthermore, EP 1148065 A1, teaches the construction and use of soluble gp130 fusion proteins. As this term is used in the art, a fusion protein is defined as a recombinant, hybrid molecule composed of parts of two or more different molecules. In EP 1148065 A1, the fusion proteins are composed of the extracellular portion of the gp130 molecule fused to an immunoglobulin Fc portion, (Abstract, paragraphs 0001, 0013, and 0014). The instant claims do not recite the construction or use of fusion molecules.

In summary, EP 1148065 A1 does not anticipate or suggest the construction or use of IL-6/sIL-6R complex inhibitory molecules that comprise of the D1-D3 domains of gp130. Therefore, Applicants respectfully request the withdrawal of the rejection of claims 1-5, 12 under 35 U.S.C. § 102(b).

V. Claim Rejections – 35 U.S.C. § 103

A. Claims 1-6, 12, are rejected under 35 U.S.C. § 103(a) over EP 1148065 A1 in view of Patton et al.

Claims 1-6, 12, are rejected under 35 U.S.C. § 103(a) as unpatentable over EP 1148065 A1 (2001) in view of Patton et al (U.S. Patent No. 6,838,076). Allegedly, EP 1148065 A1 teaches all limitations except that "the reference does not teach that in the polypeptide-dimer the two soluble gp130 molecules are linked to each other through a forked polyethylene glycol." Patton et al. is alleged to supply the missing limitation. Applicants traverse the rejection.

Applicants respectfully assert that as explained in Section IV. above, EP 1148065 A1 is not an applicable reference since it does not teach or suggest the construction or use of gp130 polypeptide-dimers that comprise of the D1-D3 extracellular domains. The missing limitations are not supplied by Patton et al. Consequently, all of the claim limitations are not present and a case for obviousness cannot be made.

Furthermore, Patton et al. discloses the use of forked polyethylene glycol in the context of derivatized monomeric insulin. Even though Patton et al. uses the term "insulin dimer" it is defined as a disubstituted insulin molecule (col. 12, lines 7-18). In other words, an insulin dimer is not composed of two insulin molecules joined together by a polyethylene glycol molecule, forked or otherwise. Rather, an insulin dimer of Patton et al. is an insulin molecule that has two covalently bound polyethylene glycol attached. Consequently, Patton et al. does not teach or suggest the formation of dimeric gp130 molecules through the use of a forked polyethylene glycol. Additionally, Patton et al. teaches away from the production of dimers by characterizing insulin dimers as a chemical degradation product that may be responsible for the induction of immunogenicity to insulin (col. 1, lines 48-62). Clearly something to be avoided.

Since EP 1148065 A1 and Patton et al. do not teach or suggest all the claim limitations of the pending claims 1-6 and 12, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 103(a).

B. Claims 1-5, 7, 12, are rejected under 35 U.S.C. § 103(a) over EP 1148065 A1 (2001) in view of Cousens et al.

Claims 1-5, 7, 12, are rejected under 35 U.S.C. § 103(a) as unpatentable over EP 1148065 A1 (2001) in view of Cousens et al (U.S. Patent No. 4,751,180). Allegedly, EP 1148065 A1 teaches all limitations except that "the reference does not teach that in the polypeptide-dimer the two soluble gp130 molecules are linked to each other through a flexible peptide linker." Cousen et al. is alleged to supply the missing limitation. Applicants traverse the rejection.

Applicants respectfully assert that as explained in Section IV. above, EP 1148065 A1 is not an applicable reference since it does not teach or suggest the construction or use of gp130 polypeptide-dimers that comprise of the D1-D3 extracellular domains. The missing limitations are not supplied by Cousen et al. Consequently, all of the claim limitations are not present and a case for obviousness cannot be made.

Applicants, therefore, request that the rejection of claims 1-5, 7, and 12 under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

Applicants submit that this paper fully addresses the Office Action mailed August 1, 2008. Should the Examiner have any questions, the Examiner is encouraged to contact the undersigned attorney at (650) 565-3585.

FEE AUTHORIZATION

The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. **23-2415** (Docket No. 31304-763.831).

Respectfully submitted,

Date: November 3, 2008

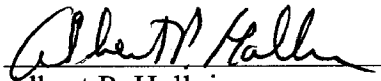
By: 

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EXHIBIT 1

The Journal of Immunology, 2000, 164: 273-282.

Importance of the Membrane-Proximal Extracellular Domains for Activation of the Signal Transducer Glycoprotein 130[1]

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The transmembrane glycoprotein gp130 is the common signal transducing receptor subunit of the IL-6-type cytokines. The gp130 extracellular part is predicted to consist of six individual domains. Whereas the role of the three membrane-distal domains (D1–D3) in binding of IL-6 and IL-11 is well established, the function of the membrane-proximal domains (D4–D6) is unclear. Mapping of a neutralizing mAb to the membrane-proximal part of gp130 suggests a functional role of D4–D6 in receptor activation. Individual deletion of these three domains differentially interferes with ligand binding of the soluble and membrane-bound receptors. All deletion mutants do not signal in response to IL-6 and IL-11. The deletion mutants Δ4 and, to a lesser extent, Δ6 are still activated by agonistic monoclonal gp130 Abs, whereas the deletion mutant Δ5 does not respond. Because membrane-bound Δ5 binds IL-6/soluble IL-6R as does wild-type gp130, but does not transduce a signal in response to various stimuli, this domain plays a prominent role in coupling of ligand binding and signal transduction. Replacement of the fifth domain of gp130 by the corresponding domain of the homologous G-CSF receptor leads to constitutive activation of the chimera upon overexpression in COS-7 cells. In HepG2 cells this mutant responds to IL-6 comparable to wild-type gp130. Our findings suggest a functional role of the membrane-proximal domains of gp130 in receptor activation. Thus, within the hematopoietic receptor family the mechanism of receptor activation critically depends on the architecture of the receptor ectodomain.